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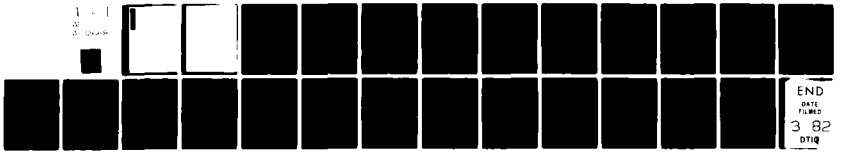

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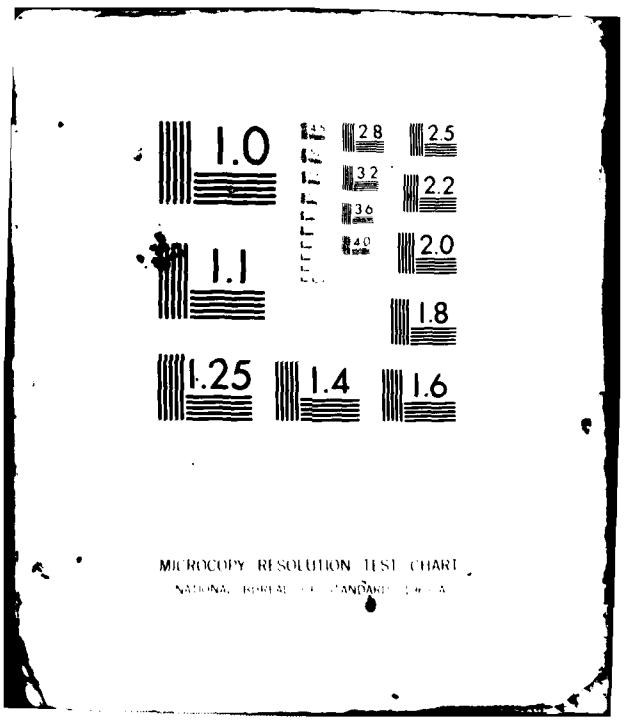
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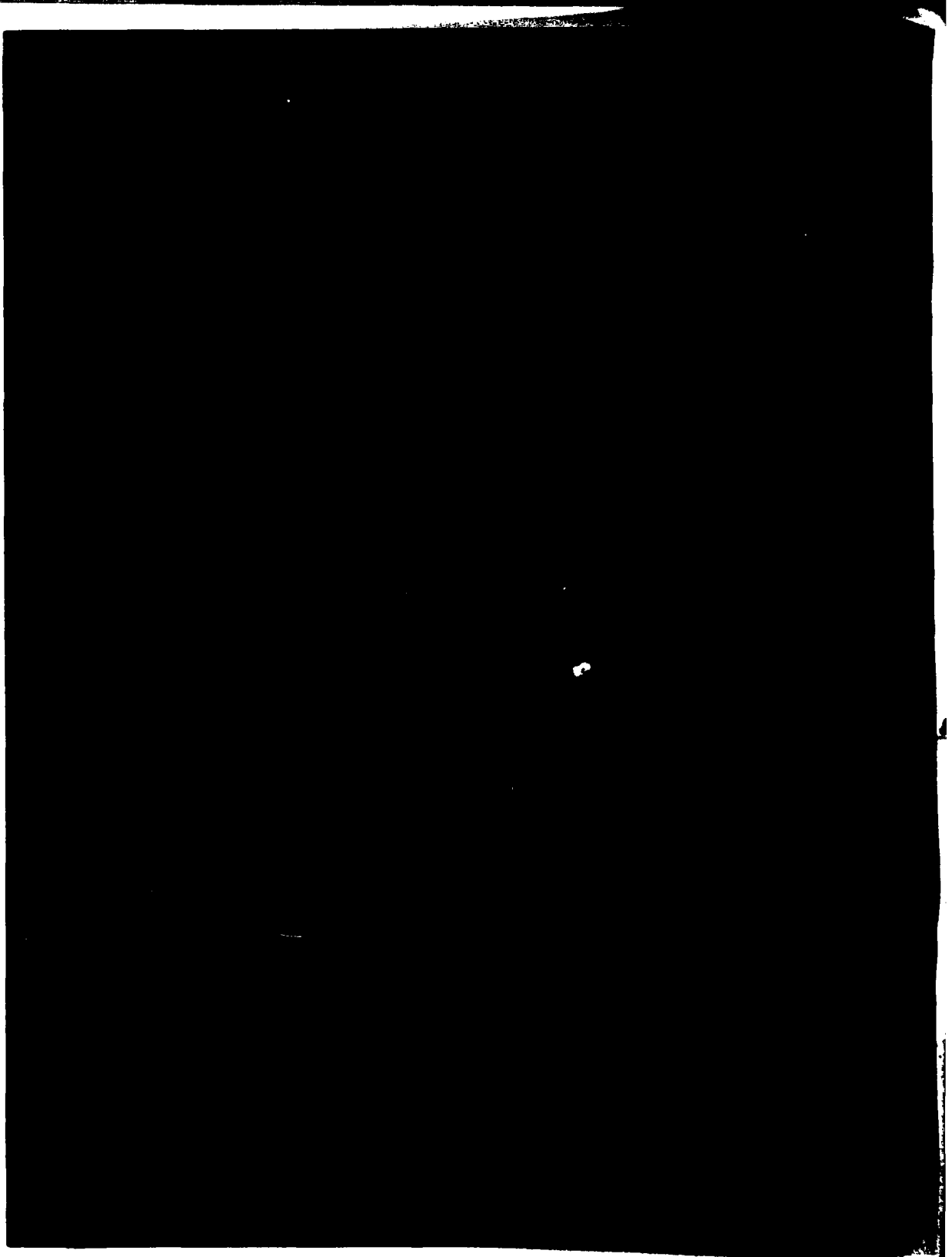

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Blood chemistry	Particle size	Smoke screen
$B_6C_3F_1$ mice	Pathology	Subchronic toxicity
Data base	PEG 200	Toxicology of smoke
Fischer-344 rats	Physiology	Training agent
Hematology	Polyethylene glycol 200	

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

In this study mice and rats were repeatedly exposed to concentrations of either 100 mg/m^3 or 1000 mg/m^3 of PEG 200 aerosol for 6 hours a day, 5 days a week, for up to 13 weeks. The mice and rats did not appear to have any lesions related to the experimental procedure. No biologically consistent significant alterations in blood chemistry, hematology, or

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-pulmonary resistance were found. No mutations or pathological abnormalities could be attributed to exposure to PEG 200. The data resulting from these studies may be useful in the derivation of airborne control limits for protection of personnel.

PREFACE

The work described in this report was authorized under Project Number 1L162622A554-4E. The work was started in October 1979 and completed in October 1980.

The experimental data are contained in notebooks 9699, 10,069, and 810057. Data from blood tests are computerized in the Toxicology Branch, Research Division, Chemical Systems Laboratory. Pathological findings are recorded in a pathology accession book and a yearly protocol book, and are computerized in the Comparative Pathology and Surgery Branch, Biomedical Laboratory.

In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals" as promulgated by the Committee on Revision of the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Resources - National Research Council.

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The authors also wish to acknowledge the assistance of Messrs. Paul D. Jacobs, James E. McWayne, and Robert M. Briscoe for the care and feeding of the animals used in this study.

CONTENTS

LIST OF TABLES

TABLE

THE SUBCHRONIC INHALATION TOXICITY OF POLYETHYLENE GLYCOL 200 IN THE RAT AND MOUSE

1. INTRODUCTION

One of the missions of the Toxicology Branch, Research Division, is to develop a toxicological data base of chemical compounds. This data base is compiled from studies conducted with laboratory animals to aid in predicting the possible hazardous effects in man. Subchronic inhalation studies are conducted to determine what risks are incident to long-term exposures in order to provide appropriate safety guidelines.

Polyethylene glycol 200 (PEG 200) is one of the candidates selected for toxicological evaluation in the Smoke Toxicology Program. It is a dihydroxy derivative of the paraffins. Polyethylene glycol formula weights range from 200 to 10,000. The physical state ranges from water-white liquids (PEG 200) to waxy solids (Carbowax^{R}). Polyethylene glycols are used extensively in industry as lubricants, plasticizers, binders, and similar applications. In the pharmaceutical industry, polyethylene glycols are widely used as components of water-soluble ointment bases, soluble dressings for wounds, carriers for penicillin, sulfa drugs, and peroxides, and in suppositories, where they serve as the base and the carrier. In cosmetics, they are used in skin conditioning creams, aqueous hair dressing, and as solvents for dyes used in lipsticks.

Literature searches and preliminary and acute toxicity studies conducted by Chemical Systems Laboratory[1] indicate PEG 200 to be nontoxic. The members of a Chemical Selection Working Group of the National Cancer Institute, in a meeting on 28 June 1979, decided that PEG 200 was not a potential carcinogen. They also stated that a wide range of polyethylene glycols (e.g., 200, 400, 1540, 4000) have been tested and generally found to be non-suspicious. There is no available data on the inhalation hazards of PEG 200 aerosols.

PEG 200 is a prime candidate as a safe training smoke for use with unmasked personnel, and also as a screening smoke to replace fog oil which may contain possible carcinogens. It was selected as a fill for the UK Simulator, Projectile, Airburst, Liquid (SPAL) training system which has been adopted by the US Army. The Army Surgeon General approved this usage provided that protective clothing and masks are worn throughout the test periods by personnel subject to repeated exposures, and that protective clothing (masks at "ready" position) are used by all other personnel. Approval was also granted for the use of aerial spray tanks in chemical defense training exercises.

This study was performed to reveal any toxicological effects which might result from repeated, long-term exposure to airborne concentrations of PEG 200. Observations were conducted in rats and mice for toxicological, physiological, hematological, blood chemical, and pathological effects. The effects of PEG 200 on the rat reproductive system were studied and will be reported later.

2. EXPERIMENTAL PROCEDURES

2.1 Description of PEG 200. Polyethylene glycol 200 has the general formula $H(OCH_2CH_2)_nOH$ where n is greater than or equal to 4. Its molecular weight is 190-210. The specific gravity is 1.125 (25°C). PEG 200 will not hydrolize or deteriorate during storage nor support mold growth.

2.2 Description of Animals. The Fischer 344 rats* were young adults at the beginning of the experiment. Males weighed approximately 115 gm and females approximately 77 gm.

The mice, $B_6C_3F_1$,** were young adults at the start of the experiment. Males weighed approximately 30 gm and females approximately 25 gm. All animals were selected, quarantined, and examined before issue by personnel of the Veterinary Resources Branch, Veterinary Medicine Division, Biomedical Laboratory.***

2.3 Exposure Protocol. The caged animals were exposed in two 3,000-liter dynamic airflow chambers;[2] one contained 100 mg/m3 of PEG 200 and the other contained 1000 mg/m3 of PEG 200. These concentrations were maintained for 6 hours a day, 5 days a week, for 13 weeks (excluding holidays). A third 3000-liter chamber was utilized for the control rats and mice. The control animals were handled and cared for in the same manner as the exposed animals except that they were not exposed to PEG 200. All three chambers are located in room 137, building E3222. This building is air conditioned and temperature and humidity are maintained at a constant level.

The rats and mice were exposed in compartmented stainless-steel wire mesh cages. Each compartment in the rat cage measured 7-1/2 in. by 3-1/2 in. by 3-1/4 in. Each mouse cage compartment measured 3 in. x 2 in. x 2-1/4 in. The compartments were labeled with a number so that each animal was in the same cage and compartment for the daily exposures. Following the 6-hour exposure, the caged animals were removed from the chambers, placed on carts and carried to adjoining holding rooms. One room was for control and another room was for exposed animals. The animals were removed from the exposure cages and placed in individually labeled stainless-steel mesh holding cages. Rat holding cages measured 9-1/2 in. x 6-3/4 in. x 7 in. Mouse holding cages measured 9-1/2 in. x 4 in. x 5 in. Food and water was available to the animals only while in the holding cages and not during PEG 200 exposures. The animals were sex-segregated at all times.

The exposed and control animals were observed daily for toxic signs and death. They were weighed biweekly and at that time were scrutinized more critically for toxic signs.

A total of 90 mice were required, 30 to be exposed to the high-dose level, 30 to the low-dose level, and 30 to serve as controls. Each of these groups were divided into three subgroups:

(a) Six-week exposure group of 10 animals
(b) Thirteen-week exposure group of 10 animals
(c) A group of 10 animals to be held for 30 days after the 13-week exposure

Pathological and hematological examinations were performed on the respective groups at the termination of the exposure-holding periods.

Rats were divided in the same manner as the mice. The total number of rats, however, was increased from 90 to 216 to provide a group of sufficient size for physiological and behavioral evaluations. Such effects were measured in one-half of the animals. Control animals underwent sham exposures. Rats evaluated for physio-

* The rats were purchased from The Charles River Breeding Laboratories, Inc. 251 Ballard Vale St., Wilmington, MA 01887.
** The mice were purchased from Harlan Industries, Inc., Box 29176, Indianapolis, IN 46229.
*** Now the USA Medical Research Institute of Chemical Defense.

logical and behavioral effects were not routinely necropsied. Some were examined if the results of the physiological evaluation warranted pathological verification of compound effects. Blood chemistry and hematological evaluations were only performed on the rats normally scheduled for necropsy. An additional 200 rats were exposed to study the effects on the reproductive process; the results will be reported separately. Methodology for these various evaluations has been approved by the Laboratory Animal Care and Use Committee of the Chemical Systems Laboratory. Test schedules are shown in tables 1 and 2.

2.4 Hematology and blood chemistry. The animals were anesthetized with ip pentobarbital sodium and blood samples taken by cardiac puncture. The following hematological blood parameters* were evaluated: red blood cells, white blood cells, differential white count, hemoglobin and hematocrit. The following blood chemistry parameters were evaluated: glucose, urea nitrogen, creatinine, sodium, potassium, chloride, carbon dioxide, uric acid, total protein, albumin, globulin, calcium, phosphate, cholesterol, triglycerides, alkaline phosphatase, glutamic oxalacetic transaminase, glutamic pyruvic transaminase, lactic dehydrogenase, and total bilirubin.

Because of the small amount of blood obtainable from the mice, only hemograms were determined for this species.

2.5 Physiological measurements (rats). A physiological evaluation was performed on control low-dose (100 mg/m^3) and high-dose (1,000 mg/m^3) rats exposed to aerosolized PEG-200 for 6 and 13 weeks and on control low- and high-dose groups kept for 30 days after the 13-week exposure. The exposure chambers and conditions of exposure are described in section 2.3.

At the end of the exposure, the rats were taken to the laboratory where they were weighed, returned to their home cages and allowed to acclimatize overnight. . During the following 2 days they were examined and tested according to the guidelines published by Cummings *et al.*[3] These included measurements of temperature, EKG, heart rate, blood pressure, ventilation, physical performance, and reflex activity. The effects of the exposure on pulmonary function and behavior are given in a later section. EKG's were analyzed for wave amplitudes, intervals, duration, rhythm and axis. Pulmonary ventilation was analyzed for frequency, volume, and changes due to breathing 6% carbon dioxide. The measurements described[3] were all performed on unanesthetized and comfortably restrained rats.

The data were compared statistically using an analysis of variance (ANOVA) which distinguished differences according to sex, exposure level, and the effect of dose within sexes.

The logic for determining a physiological effect from the PEG 200 aerosol required that the following conditions be considered:

1. a significant difference at the P = 0.05 level had to be evidenced by the analysis of variance;

*The hematology and blood chemistry analyses were done on contract by the National Health Laboratory, Inc., 1007 Electric Ave., Vienna, Virginia, 22180.

Table 1. Test Schedule for Subchronic Exposures of Mice to PEG 200

Sex	Dose	Number submitted for necropsy*		
		6 Week (17 - 18 December 1979)	13 Week (4 - 5 February 1980)	30 day postexposure (3 - 4 March 1980)
M	Control	5 (1-5)	5 (7-11)	5 (13-17)
F	Control	5 (1-5)	5 (7-11)	5 (13-17)
M	Low (100 mg/m^3)	5 (19-23)	5 (25-29)	5 (31-35)
F	Low (100 mg/m^3)	5 (19-23)	5 (25-29)	5 (31-35)
M	High (1000 mg/m^3)	5 (37-41)	5 (43-47)	5 (49-53)
F	High (1000 mg/m^3)	5 (37-41)	5 (43-47)	5 (49-53)
		30	30	30

*Numbers in parentheses are animal identification numbers.

Table 2. Test Schedule for Subchronic Exposures of Rats to PEG 200

Sex	Dose	Number submitted for necropsy or physiological evaluation*					
		Pathology	Chemical/ physiological toxicity section	Pathology	Chemical/ physiological toxicity section	Pathology	Chemical/ physiological toxicity section
M	Control	6 (1-6)	6 (7-12)	6 (13-18)	6 (19-24)	6 (25-30)	6 (31-36)
F	Control	6 (1-6)	6 (7-12)	6 (13-18)	6 (19-24)	6 (25-30)	6 (31-36)
M	Low (100 mg/m^3)	6 (37-42)	6 (43-48)	6 (49-54)	6 (55-60)	6 (61-66)	6 (67-72)
F	Low (100 mg/m^3)	6 (37-42)	6 (43-48)	6 (49-54)	6 (55-60)	6 (61-66)	6 (67-72)
M	High (1000 mg/m^3)	6 (73-78)	6 (79-84)	6 (85-90)	6 (91-96)	6 (97-102)	6 (103-108)
F	High (1000 mg/m^3)	6 (73-78)	6 (79-84)	6 (85-90)	6 (91-96)	6 (97-102)	6 (103-108)
		36	36	36	36	36	36

*Numbers in parentheses are animal identification numbers.

2. the differences had to be dose related and directional so that significant differences occurring in a lower dose group that were not reinforced by similar effects in the high-dose groups would be considered a chance occurrence; and

3. any differences should be time-related unless an adaptive response had developed. In such a case the statistical judgments and discussion would reflect this possibility, particularly where other evidence was involved.

In addition to the physiological measurements previously described, pulmonary function tests were conducted on the Fischer 344 rats.

Pulmonary function was evaluated using the whole body plethysmographic method. This technique is used extensively for investigating the effects of airborne materials on the lungs of small (unanesthetized) animals. This technique involves the measurement of the respiratory flow, with a pneumotachometer, and the plethysmographic pressure changes during a series of normal respiratory cycles. The respiratory rates and an estimate of the pulmonary resistance can be determined from the data obtained.

In this study the rats were exposed to two dose levels of PEG 200 for a total period of 13 weeks. Pulmonary function tests were done at 6 and 13 weeks of exposure, and 30 days following the final exposure. A group of control rats (six males and six females) were tested with each group of exposed animals (six males and six females where possible). The exposed and control groups were compared statistically using the standard "t" test. Comparisons were made with controls for each test period and to the grouped controls.

2.6 Pathological evaluation. Groups of male and female rats and mice were euthanatized following 6 and 13 weeks of exposure to PEG 200 aerosol. Another group of rats and mice was euthanatized 30 days after exposure to PEG 200. At termination and necropsy, tissues were evaluated grossly and preserved in 10% buffered formalin. The tissues were imbedded in paraffin and subsequently processed for staining with hematoxylin and eosin. Tissues from the following were evaluated microscopically:* brain, eye, adrenal, thyroid, trachea, lung, turbinates, kidney, liver, spleen, heart, esophagus, stomach, small intestine, large intestine, pancreas, urinary bladder, testes, ovaries, and uterus. Before fixing the hearts, lungs, livers, kidneys, and gonads, they were weighed, and organ-to-body-weight ratios were calculated.

2.7 Operation of exposure chambers and analysis of content. Exposures were conducted in two 3,000-liter dynamic flow stainless-steel chambers operated under negative pressure. Air was drawn into the system and PEG 200 aerosol was dispersed into the intake air and passed through collective protective filters before exiting into the atmosphere. Chamber design

*Microscopic evaluation was done on contract by DVM Pathology Associates, P.O. Box 5204, Mississippi State, MS 39762.

assured that the airborne concentration of PEG 200 was uniform. The chamber airflow was held constant throughout the test at 880 liters per minute for the low-dose (100 mg/m^3) and 490 liters per minute for the high-dose (1,000 mg/m^3). This flow rate was used to calculate the nominal PEG 200 concentration.

PEG 200 aerosol was generated using 16-gauge, air-operated, opposed, jet-feed Laskin generators. Air pressure through the generators was adjusted to achieve the different test concentrations of PEG 200. For the low-dose chamber, only one generator was required to obtain the desired PEG 200 concentration; however, two generators were needed to obtain the PEG 200 concentration in the high-dose chamber.

Aerosol concentrations of PEG 200 were monitored by collecting air samples on probes that were inserted into ports on the side of the chamber wall. The probe contained two previously weighed Gelman filter pads. Samples were collected at the rate of 5 liters per minute until 60 liters were obtained. Three samples were collected during the 360-minute exposure period, usually at 90, 198, and 285 minutes. After sampling, the filter pads were removed from the probe and placed in a sample bottle, which was labeled and given to a chemist for reweighing of the filter pads to determine the weight gain. The filter pads were subsequently analyzed by a gas chromatographic method. A listing of the various requirements for GC analysis of PEG 200 is shown below.

Sample solvent	Methanol
Instrument	Hewlett-Packard Model 5730
Automatic injector	Model 7671A
Integrator	Model 3380A
Column:	Coiled Glass
ID	2 mm
Length	2.5 ft
Column packing	GC tenax, 60/80 mesh
Gas flows:	
Hydrogen	40 psig at regulator,
Nitrogen	40 psig at regulator, 15 to 18 ml/min at detector
Air	50 psig at regulator

Temperatures:

Injection port	320°C
Detector	320°C
Oven	Temperature program Time 1 = 2 min Temp 1 = 200°C Temp 2 = 280°C Time 2 = 4.0 min Rate = 15°C/min

The actual mean concentrations found for PEG 200 by analytical, nominal, and gravimetric techniques were:

Concentration group*	Analytical technique	Nominal technique	Gravimetric technique
mg/m^3	mg/m^3	mg/m^3	mg/m^3
100	94 ± 38.7	116 ± 16.0	122 ± 26
1000	727 ± 227.2	1030 ± 214.6	1001 ± 201.4

*For the sake of simplicity, the target concentrations are used throughout the report.

2.8 Body weights. The animals used in the PEG 200 study were weighed individually at approximately 2-week intervals. The average weights for the various groups, i.e., males and females for the controls, low- and high-dose levels, were recorded.

3. RESULTS

3.1 Toxic Signs. No obvious pattern of overt toxic signs was seen in the rats or mice exposed to either 100 or 1000 mg/m^3 of PEG 200. After each exposure, the fur of the animals exposed to the high dose appeared oily.

3.2 Mortality. None of the test rats died during the 13-week exposure or the 30-day postexposure observation, and none of the deaths that occurred in the $B_6C_3F_1$ mice were attributed to PEG 200.

3.3 Hematology and blood chemistry.

3.3.1 Hematology. During the 13-week exposure or the 30-day postexposure period there were no consistently significant changes in red blood cell count, total and differential white blood cell count, hematocrit, or hemoglobin in the rats or mice.

3.3.2 Blood chemistry. There were no consistently significant changes in rat blood chemistry at the end of the 6- or 13-week exposures or the 30-day postexposure period.

3.4 Physiological measurements (rats). The main physiological differences in groups were found between male and female animals, and these differences, as in ventilation, are most probably related to the size difference between the sexes. Female rats exhibited a higher rectal temperature and a slightly lower systolic blood pressure. At the 6-week exposure point, the low-dose (100 $mg/^3$) female rats showed a higher systolic blood pressure than the control animals. Since this did not occur in the high-dose animals and was not repeated in subsequent exposures, it appeared to be a chance occurrence.

In male rats exposed for 13-weeks to the high dose, there appeared to be a slight decrease in the P-R interval in the EKG compared to the control animals. The usual abnormality associated with the P-P interval is an increase in duration, which indicates a slowing of the atrial conduction system. This interval will vary inversely with heart rate, but heart rate did not appear to be a factor in the present study. In any event, the decrease was not associated with any abnormality and may be considered inconsequential.

PEG 200 did not product any adverse physiological effects on the rats exposed to the 100 and 1000 mg/m^3 concentrations for the various exposure periods. This was not unexpected because the polyethylene glycols appear to present slight industrial hazard. Although little is known on the inhaled effects, the PEG series are relatively nonirritating to eyes, skin, and mucous membranes.[4]

The results of the pulmonary tests, summarized in table 3, include the respiratory rate, extimated pulmonary resistance, and respiratory flow rate. The results indicate that these dose levels of PEG 200 for a period of 13 weeks had no effect on the pulmonary function of the rat. Female rats exhibited some change after the 6-week exposure to 1000 mg/m^3; the statistical differences were not significant. However, four out of the five animals showed a decrease in respiratory rate and an increase in estimated pulmonary resistance. These changes were apparently transient since they were not apparent in the males, nor at 13 weeks and 30 days postexposure in the females.

3.5 Body weights. There was no definite pattern in the body weights of male or female mice. There were weeks when the average weights of the exposed animals were slightly less or greater than the control weights. Both male and female exposed mice weighed more than the controls during the 30-day postexposure period. Fischer 344 exposed rats, both males and females, showed no definite pattern as to weight loss or gain. At the end of the postexposure period the rats weighed as much as, or slightly greater than, the controls.

Table 3. Summary of the Pulmonary Function Tests in Rats Exposed to Two Dose Levels of PEG 200 for 13 Weeks (Mean ± SD)

Exposure	n	Rate (breaths/minute)	Flow (ml/sec)	Estimated pulmonary function (cm H_2O/l/sec)
			Females	
6 weeks				
Control	6	191 ± 5.2	16.3 ± 0.64	59.96 ± 2.47
100 mgm/m^3	6	202 ± 10.9	15.4 ± 0.45	52.54 ± 1.99
1000 mgm/m^3	5	131 ± 42.3	13.8 ± 2.61	71.81 ± 15.22
13 weeks				
Control	6	162 ± 7.8	17.0 ± 0.58	48.82 ± 1.16
100 mgm/m^3	6	169 ± 4.5	17.8 ± 0.48	45.17 ± 1.23
1000 mgm/m^3	6	162 ± 2.3	17.6 ± 0.55	53.95 ± 5.77
30 days postexposure				
Control	6	173 ± 6.5	16.5 ± 1.18	50.71 ± 4.26
100 mgm/m^3	5	174 ± 6.3	16.4 ± 0.30	55.38 ± 1.00
1000 mgm/m_3	6	178 ± 5.0	17.7 ± 0.46	47.72 ± 1.14
Grouped controls	18	175 ± 4.6	16.6 ± 0.46	53.16 ± 1.98
			Males	
6 weeks				
Control	6	116 ± 12.9	16.6 ± 0.42	100.02 ± 5.42
100 mgm/m^3	6	117 ± 16.2	16.2 ± 0.57	91.10 ± 6.72
1000 mgm/m^3	6	115 ± 13.8	16.0 ± 1.27	95.13 ± 7.41
13 weeks				
Control	6	154 ± 4.3	17.8 ± 0.39	65.53 ± 2.92
100 mgm/m^3	6	153 ± 9.3	18.1 ± 0.93	81.92 ± 11.97
1000 mgm/m^3	6	159 ± 7.6	20.0 ± 0.75	81.59 ± 2.37
30 days postexposure				
Control	6	135 ± 7.2	17.8 ± 0.83	89.90 ± 1.11
100 mgm/m^3	6	130 ± 11.0	18.1 ± 0.95	89.12 ± 3.73
1000 mgm/m^3	6	148 ± 11.2	19.9 ± 0.79	81.59 ± 2.36
Grouped control	18	135 ± 6.1	17.4 ± 0.35	85.16 ± 4.02

3.6 Pathology.

3.6.1 Light microscopy.

Control animals, mice and rats, were used for both the low (100 mg/m^3) and high (1000 mg/m^3) dose levels of PEG 200.

3.6.1.1 Mice - 6 weeks. Interstitial pneumonia was found in three low dose mice (one male, two female). Atelectasis was observed in the lungs of a male and a female control. This probably reflects improper inflation during the necropsy procedure. Adrenal cortical degeneration was seen in a control female. Renal tubular vacuolar degeneration was seen in all of the male mice. Mild degenerative changes were observed in the liver of one female mouse exposed to the high dose. Cystic endometrial hyperplasia (minimal-mild) was found in 10 females (5 controls, 5 exposed).

One male control mouse died spontaneously at the end of 6 weeks. No significant microscopic lesions were found. There was a swollen area in the cervical region, probably due to accidental injury when the mouse was loaded into the cage.

3.6.1.2 Rats - 6 weeks. Mild to moderate proliferative interstitial pneumonia was seen in nine rats, (three control males, five exposed males (two low- and three high-dose), and one female - low-dose. Acute to subacute inflammation of the turbinates was observed in one control female and two exposed (low-dose) males.

3.6.1.3 Mice - 13 weeks. Infiltration of foamy macrophages in the lung, a common incidental finding in rodents, was found in one exposed (low-dose) male. Interstitial pneumonia occurred in four mice (two males and one female control and one male - high-dose). Renal tubular degeneration was again observed in all of the male mice. Cystic endometrial hyperplasia was noted in 10 females (5 controls - 4 low-dose and 1 high-dose). Endomitriosis was found in one low-dose mouse. No spontaneous deaths occurred.

3.6.1.4 Rats - 13 weeks. Infiltration of foamy macrophages occurred in the lungs of one exposed (high-dose) male. Suppurative inflammation of the turbinates was seen in a control female. A renal cortical cyst was found in one control female. No spontaneous deaths occurred.

3.6.1.5 Mice - 13-week exposure plus 30-day postexposure. Adrenal cortical degeneration was found in one exposed (low-dose) female. Interstitial pneumonia occurred in four males (one control, two low, one high-dose). Infiltration of foamy macrophages was seen in the lung of one exposed (high-dose) male. Tubular degeneration was identified in all males. Endometrial cysts were found in 12 females (5 controls, 4 low-, 3 high-dose). Hydronephrosis was found in one exposed (high-dose) male. No spontaneous deaths occurred.

3.6.1.6 Rats - 13-week exposure plus 30-day postexposure. Infiltration of foamy macrophages occurred in three females (one control, one low-, one high-dose). One exposed (low-dose) female exhibited mild turbinate inflammation. Inflammation of the renal pelvis was seen in one exposed (high-dose) female. No spontaneous deaths occurred.

3.6.2 Summary. No significant lesions observed in this study occurred exclusively in exposed animals and the severity of lesions which were found was not dose-related. It is our impression that there were no PEG 200 induced lesions in rat or mouse tissue at the dosage levels and exposure/postexposure periods evaluated in this study.

3.6.3 Organ:body weight ratios. Organ:body weight ratios in rats at all concentrations and for the 6- and 13-week exposure periods and the 30-day postexposure period showed no pattern of significance that could be related to PEG 200. The mice organ:body weights for the 6-week exposure period are unavailable. No pattern of significance could be related to PEG 200 exposure for the 13-week or the 30-day postexposure periods.

3.7 Chamber data and weekly cumulative Ct's.

3.7.1 Chamber data. Based on daily recordings, the mean room temperature and standard deviation for room 137, building E3222, where these tests were conducted, was 71.4° ± 1.3°F. The room humidity was 27.2% ± 5.4%.

Particle size measurements of the PEG 200 aerosol were obtained by using a modified Rochester cascade impactor. The particle size for the high-dose (1000 mg/m^3) chamber was 0.71 µ MMD, and 0.80 µ MMD for the low-dose (100 mg/m^3) chamber. These particle sizes were based on data obtained from gas chromatographic analysis of the six stages of the cascade impactor. A typical aerodynamic size distribution is presented in table 4.

3.7.2 Cumulative Ct's. The total cumulative Ct's (milligram minutes per cubic meter) for the gas chromatographic technique after 13 weeks of exposure to PEG 200 aerosol was lower than the nominal and gravimetric techniques. This may be due to the fact that the nominal technique does not take into account the disposition of aerosol particles upon the walls of the chamber, the animal cages, or the hair of the animals. The gravimetric method does not exclude moisture in the air that may be collected on the filter pads during the sampling procedure.

4. CONCLUSIONS

4.1 Rats and mice were exposed to airborne concentrations of 100 and 1000 mg/m^3 of PEG-200 for periods up to 13 weeks. Toxicological, physiological, hematological, blood chemical, and pathological effects were evaluated during the course of the exposures.

4.2 It appears that PEG-200 produced no positive effects in the rodents at the 100 and 1000 mg/m^3 PEG-200 concentrations over the 13 weeks of exposure used in this study.

Table 4. Particle Size Distribution of PEG 200 Aerosols Collected on a Modified Rochester Cascade Impactor

Impactor Collection Stage	Aerodynamic Particle Diameter - 50% Cut-Off	Mass Collected	Cumulative Percent
	microns	mg	
1	10.9	0	---
2	4.8	1.7	100.0
3	2.3	0	88.8
4	1.3	2.1	88.8
5	0.74	9.1	74.9
6	0.41	2.2	14.6

Plotting cut-off diameter and cumulative percent on log probability yields a mass median diameter of 0.71 microns, geometric standard deviation 1.97

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